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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/549,528

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Shawn De Frees

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EXAMINER

HEARD, THOMAS SWEENEY

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

01/06/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/549,528	Applicant(s) DE FREES, SHAWN	
	Examiner THOMAS S. HEARD	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 13, 15, and 17-23 is/are pending in the application.
- 4a) Of the above claim(s) 18 and 19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 13, 15 and 17-23 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

The Applicants Amendments to the claims received on 9/30/2008 is acknowledged. The text of those sections of Title 35 U.S. Code not included in the action can be found in the prior office action. Rejections or objections not addressed in this office action with respect to the previous office action mailed 3/31/2008 are hereby withdrawn.

Claim(s) 1-10, 13, 15, and 17-23 are pending. Applicants have amended claim(s) 1, 13, 15, 17, and added Claims 20-23. Claims 18 and 19 are withdrawn. Claims 1-10, 13, 15, 17, and 20-23 are hereby examined on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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For the purpose of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. *Joy Technologies Inc. V. Quigg*, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held in accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. *In re Hoeschele*, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. *In re Clinton*, 188 USPQ 365, 367 (CCPA 1976); *In re Thompson*, 192 USPQ 275, 277 (CCPA 1976).

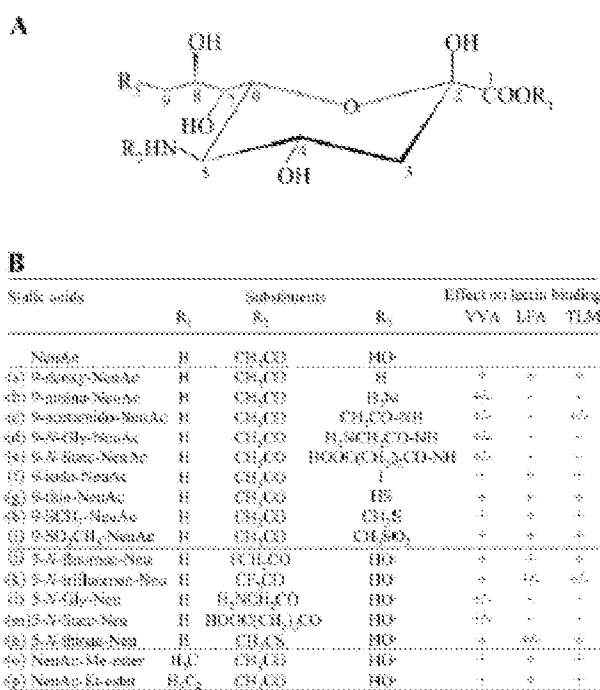
Claims 1-10, 13, 15, 17, and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeFrees et al, US 7,265,085 in light of Oetke et al, "Versatile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " *The Journal of Biological Chemistry* (2002), pages 668-6695, from Applicant's IDS..

The instant invention is drawn to a method of forming a peptide conjugate where a modified sugar is incubated under conditions where the cell internalizes the modified sugar, in incorporated into a nucleotide sugar, and is then covalently linked to the peptide through the catalysis of the glycosyltransferase present within the cell.

DeFrees, et al, US 7,265,085 discloses the plurality of compounds of Claims 15 and 20 used in a cell free method of transferring the modified sugar or nucleotide sugar to the enzymes and proteins of Claim 17, see Claim 34 and Column 13, 75 and 76 of '085 for example. DeFrees et al does not teach the *in vivo* methods instantly claimed but instead relies on *in vitro* steps with isolated enzymes to perform the method. The difference between what is taught by the prior art and that instantly claimed is that DeFrees et al teaches the *in vitro* methods of making the instant invention of water soluble modified proteins, but Oetke et al teaches *in vivo* methods of making the

compounds with modified sugars through the steps instantly claimed, but not with water soluble polymer modified sugars.

Oetke et al discloses a method of modifying a peptide/protein by incubating the cells expressing the peptide/protein with a modified sugar, which is internalized and covalently linked to the peptide through the catalysis of the glycosyltransferase present within the cell. Oetke et al teaches a variety of modification (see Figure 1A and 1B below), where substitutions were made at R₁, R₂, and R₃:



It would have been obvious to one of ordinary skill in the art to modify the compounds taught by Oetke et al and incorporate the water soluble polymer modified sugars as taught by Defrees et al. One would have been motivated to do so given the teachings from Oetke et al that the cells would take up the sugars and incorporate them

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in vivo. One would have had a reasonable expectation of success in practicing the methods as Oetke et al teaches the in vivo method instantly claimed and Defree et al teaches that the water soluble polymer modified sugars residues are also substrates for the enzymes that catalyze the reaction. From the teachings of the references supra, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, and the invention as claimed, is rejected under 35 U.S.C. 103(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10, 13, 15, 17, and 20-23 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-94 of U.S. Patent No. US 7,265,085 B2 in view of Oetke et al, "Versatile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US 7,265,085 B2 teaches the enzymatic modification of peptide and protein through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,265,085 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,265,085 does not teach an *in vivo* method of practicing the same methods of synthesis.

Oetke et al teaches a method of modifying peptides or proteins by cellular (*in vivo*) incubation with the desired modified sugar, in the instant case, polyethylene glycol. The difference between what is taught in the prior art and what is claimed is that one is done with enzymes *in vivo* rather than *in vitro*.

It would have been obvious at the time of the instant invention to modify the method instantly claimed to incorporate the *in vivo* method taught by Oetke et al. One would have had been motivated to do so given the success in incorporating modified sialic residues into proteins as taught by Oetke et al. One would have had a reasonable expectation of success given Oetke et al teaching that the modified sugar residues

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would have been taken up by the cell and incorporated by cellular enzyme native to the cell, and perform the same method instantly claimed. Therefore, the invention as claimed is prima-facie obvious of the secondary reference of Oetke et al.

Claims 1-10, 13, 15, 17, and 20-23 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 112-214 of U.S. PG Pub 20080050772 in view of Oetke et al, "Versatile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. 20080050772 teaches the enzymatic modification of granulocyte colony stimulating factor through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of 20080050772 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,265,085 does not teach an *in vivo* method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,265,085 in view of Oetke et al, it would have been obvious to modify the instant method to utilize *in vivo* methods of conjugation to make a pegylated granulocyte colony stimulating factor as claimed in the instant Claim 17

Claims 1-10, 13, 15, 17, and 20-23 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-155 of U.S.

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Patent No. US 7,297,511 in view of Oetke et al, "Versatile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US 7,297,511 teaches the enzymatic modification of interferon alpha through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,297,511 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,297,511 does not teach an *in vivo* method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,265,085 in view of Oetke et al, it would have been obvious to modify the instant method to utilize *in vivo* methods of conjugation to make a pegylated interferon alpha claimed in the instant Claim 17.

Claims 1-10, 13, 15, 17, and 20-23 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-113 of U.S.

Patent No. US 7,226,903 in view of Oetke et al, "Versatile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US 7,226,903 teaches the enzymatic modification of interferon beta through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater

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half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,226,903 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,226,903 does not teach an *in vivo* method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,226,903 in view of Oetke et al, it would have been obvious to modify the instant method to utilize *in vivo* methods of conjugation to make a pegylated interferon beta claimed in the instant Claim 17.

Claims 1-10, 13, 15, 17, and 20-23 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-32 of U.S. Patent No. US 7,214,660 in view of Oetke et al, "Versatile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues," The Journal of Biological Chemistry (2002), pages 668-6695. US 7,214,660 teaches the enzymatic modification of EPO through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,214,660 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,214,660 does not teach an *in vivo* method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,214,660 in view of Oetke et al, it would have

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been obvious to modify the instant method to utilize in vivo methods of conjugation to make a pegylated EPO claimed in the instant Claim 17.

Claims 1-10, 13, 15, 17, and 20-23 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-107 of U.S. Patent No. US 7,179,617 in view of Oetke et al, "Versatile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, " The Journal of Biological Chemistry (2002), pages 668-6695. US 7,179,617 teaches the enzymatic modification of Factor IX through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,179,617 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,179,617 \ does not teach an in vivo method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,179,617 in view of Oetke et al, it would have been obvious to modify the instant method to utilize in vivo methods of conjugation to make a pegylated Factor IX claimed in the instant Claim 17.

Claims 1-10, 13, 15, 17, and 20-23 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-94 of U.S. Patent No. US 7,173,003 in view of Oetke et al, "Versatile Biosynthetic Engineering of

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Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, “ The Journal of Biological Chemistry (2002), pages 668-6695. US 7,173,003 teaches the enzymatic modification of GCS through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also therapeutic for longer half-life). The method of the invention of US 7,173,003 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,173,003 does not teach an *in vivo* method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,173,003 in view of Oetke et al, it would have been obvious to modify the instant method to utilize *in vivo* methods of conjugation to make a pegylated GCS claimed in the instant Claim 17.

Claims 1-10, 13, 15, 17, and 20-23 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-94 of U.S. Patent No. US 7,157,277 in view of Oetke et al, “Versatile Biosynthetic Engineering of Sialic Acid in Living Cells Using Synthetic Sialic Acid Analogues, “ The Journal of Biological Chemistry (2002), pages 668-6695. US 7,157,277 teaches the enzymatic modification of Factor VII through the coupling of modified sialic acid residues, for example, where the modifying agent is a polyethylene glycol, readable, for example, upon a water soluble polymer, a therapeutic agent (allows circulatory greater half-life), a detectable moiety (molecular weight shift in SDS-PAGE gels), and a biomolecule (also

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therapeutic for longer half-life). The method of the invention of US 7,157,277 teaches the *in vitro* method using transferase enzymes purified from cellular sources. US 7,157,277 does not teach an *in vivo* method of practicing the same methods of synthesis. For the reasons set forth supra, regarding US 7,157,277 in view of Oetke et al, it would have been obvious to modify the instant method to utilize *in vivo* methods of conjugation to make a pegylated Factor VII claimed in the instant Claim 17.

Applicant's arguments for all of the double patenting rejections set forth above is that since no allowable subject matter has been indicated. Applicants will consider filing the appropriate terminal disclaimer upon indication of allowable subject matter. The rejection is maintained as the double patenting rejections cannot be held in abeyance.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Prior art contained in the reference of record can be applied in the next office action.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be

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applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Thomas S. Heard** whose telephone number is **(571) 272-2064**. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thomas S Heard/
Examiner, Art Unit 1654

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654